Amendments to the Claims

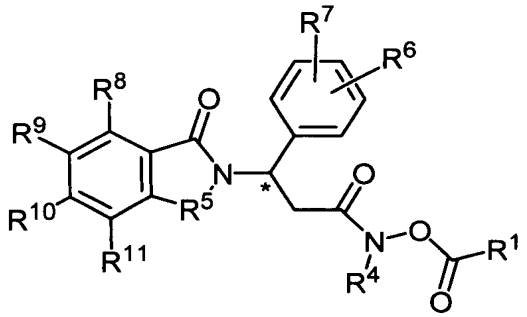
This listing of the claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-42. (Canceled).

43. (New) A pharmaceutical composition comprising:

(a) a compound of formula **I** , **II,** a pharmaceutically acceptable salt or solvate thereof, or a substantially chirally pure (R) or (S) isomer thereof:



I

wherein:

the carbon atom designated * constitutes a center of chirality;

R^4 is hydrogen or -(C=O)-R^{12};

each of R^1 and R^{12}, independently of each other, is alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridyl methyl, pyridyl, imidazoyl, imidazolylmethyl, or $CHR^*(CH_2)_nNR^*R^0$, wherein $R^*$and R^0, independently of the other, are hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridylmethyl, pyridyl, imidazoyl or imidazolylmethyl, and n = 0, 1, 2;

R^5 is C=O, CH_2, -CH_2-CO-, or SO_2;

each of R^6 and R^7, independently of the other, is nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 6 carbon atoms, alkoxy of 1 to 6 carbon atoms, cycloalkoxy of 3 to 8 carbon atoms, halo, bicycloalkyl of up to 18 carbon atoms, tricycloalkoxy of up to 18 carbon atoms, 1-indanyloxy, 2-indanyloxy, C_4-C_8-cycloalkylidenemethyl, or C_3-C_{10}-alkylidenemethyl; and

each of R^8, R^9, R^{10}, and R^{11} independently of the others, is

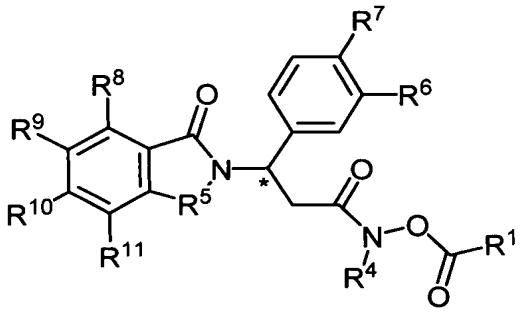
(i) hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, halo,

(ii) one of R^8, R^9, R^{10}, and R^{11} is acylamino comprising a lower alkyl, and the remaining of R^8, R^9, R^{10}, and R^{11} are hydrogen,

(iii) hydrogen if R^8 and R^9 taken together are benzo, quinoline, quinoxaline, benzimidazole, benzodioxole, 2-hydroxybenzimidazole, methylenedioxy, dialkoxy, or dialkyl,

(iv) hydrogen if R^{10} and R^{11}, taken together are benzo, quinoline, quinoxaline, benzimidazole, benzodioxole, 2-hydroxybenzimidazole, methylenedioxy, dialkoxy, or dialkyl, or

(v) hydrogen if R^9 and R^{10} taken together are benzo; or



II

wherein:

the carbon atom designated * constitutes a center of chirality;

R^4 is hydrogen or -(C=O)-R^{12},

where each of R^1 and R^{12}, independently of each other, is alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridyl, pyridyl methyl, imidazolyl, imidazoylmethyl, or $CHR^*(CH_2)_nNR^*R^0$

wherein $R^*$and R^0, independently of the other, are hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridylmethyl, pyridyl, imidazoyl or imidazolylmethyl, and n = 0, 1, 2;

R^5 is C=O or CH_2;

each of R^6 and R^7, independently of the other is alkoxy of 1 to 8 carbon atoms, cycloalkoxy of 3 to 6 carbon atoms; C_4-C_6-cycloalkylidenemethyl, C_2-C_{10}-alkylidenemethyl, C_6-C_{18}-bicycloalkoxy, C_6-C_{18}-tricycloalkoxy, 1-indanyloxy, or 2-indanyloxy;

each of R^8, R^9, R^{10}, and R^{11}, independently of the others, is hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, halo, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, and alkoxy of 1 to 10 carbon atoms; and

(b) a pharmaceutically acceptable carrier.

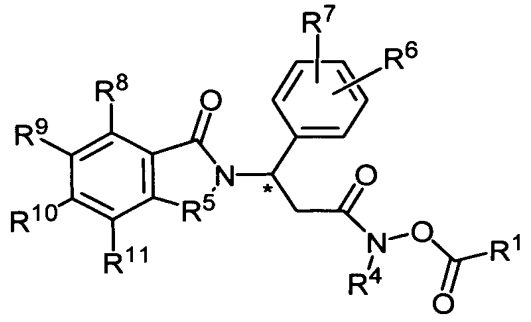
44. (New) The pharmaceutical composition of claim 43, wherein the compound is a compound of formula **I**.

45. (New) The pharmaceutical composition of claim 43, wherein the compound is a compound of formula **II**.

46. (New) The pharmaceutical composition of claim 43, wherein the compound is (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) propanoate; (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) acetate; (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) pentanoate; (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) benzoate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(1-oxoisoindolin-2-yl)propanoylamino) acetate; (3-[4-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-ethoxy-4-methoxyphenyl) propanoylamino)acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; N-acetyl-(3-(3-ethoxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; N-acetyl-(3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino) acetate; (3-[5-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) acetate; (3-(1,3-dioxobenzo[e]isoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl) propanoylamino)acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-phthalimido-propanoylamino)pyridine-3-carboxylate; (3-[4-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-cyclopentyloxy-4-methoxyphenyl)propanoylamino)acetate; (N-acetyl-3-[4-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-cyclopentyloxy-4-methoxyphenyl)propanoylamino)acetate; or (3-(3-ethoxy-4-methoxyphenyl)-3-(1-oxoisoindolin-2-yl)propanoylamino)acetate.

47. (New) A method of inhibiting PDE-4, TNF-α, MMP, or undesired angiogenesis in a mammal comprising administering to said mammal an effective amount of

a compound of formula **I, II,** a pharmaceutically acceptable salt or solvate thereof, or a substantially chirally pure (R) or (S) isomer thereof:



I

wherein:

the carbon atom designated * constitutes a center of chirality;

R^4 is hydrogen or -(C=O)-R^{12};

each of R^1 and R^{12}, independently of each other, is alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridyl methyl, pyridyl, imidazoyl, imidazolylmethyl, or $CHR^*(CH_2)_nNR^*R^0$, wherein $R^*$and R^0, independently of the other, are hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridylmethyl, pyridyl, imidazoyl or imidazolylmethyl, and n = 0, 1, 2;

R^5 is C=O, CH_2, -CH_2-CO-, or SO_2;

each of R^6 and R^7, independently of the other, is nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 6 carbon atoms, alkoxy of 1 to 6 carbon atoms, cycloalkoxy of 3 to 8 carbon atoms, halo, bicycloalkyl of up to 18 carbon atoms, tricycloalkoxy of up to 18 carbon atoms, 1-indanyloxy, 2-indanyloxy, C_4-C_8-cycloalkylidenemethyl, or C_3-C_{10}-alkylidenemethyl; and

each of R^8, R^9, R^{10}, and R^{11} independently of the others, is

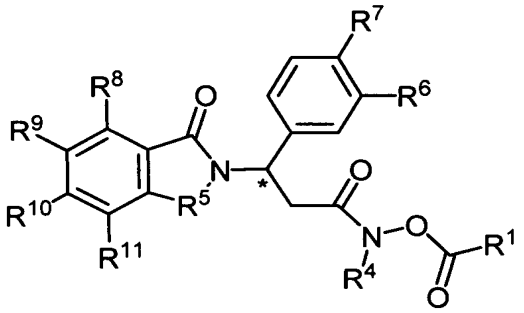
(i) hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, halo,

(ii) one of R^8, R^9, R^{10}, and R^{11} is acylamino comprising a lower alkyl, and the remaining of R^8, R^9, R^{10}, and R^{11} are hydrogen,

(iii) hydrogen if R^8 and R^9 taken together are benzo, quinoline, quinoxaline, benzimidazole, benzodioxole, 2-hydroxybenzimidazole, methylenedioxy, dialkoxy, or dialkyl,

(iv) hydrogen if R^{10} and R^{11}, taken together are benzo, quinoline, quinoxaline, benzimidazole, benzodioxole, 2-hydroxybenzimidazole, methylenedioxy, dialkoxy, or dialkyl, or

(v) hydrogen if R^9 and R^{10} taken together are benzo; or



II

wherein:

the carbon atom designated * constitutes a center of chirality;

R^4 is hydrogen or -(C=O)-R^{12},

where each of R^1 and R^{12}, independently of each other, is alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridyl, pyridyl methyl, imidazolyl, imidazoylmethyl, or $CHR^*(CH_2)_nNR^*R^0$

wherein $R^*$and R^0, independently of the other, are hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridylmethyl, pyridyl, imidazoyl or imidazolylmethyl, and n = 0, 1, 2;

R^5 is C=O or CH_2;

each of R^6 and R^7, independently of the other is alkoxy of 1 to 8 carbon atoms, cycloalkoxy of 3 to 6 carbon atoms; C_4-C_6-cycloalkylidenemethyl, C_2-C_{10}-alkylidenemethyl, C_6-C_{18}-bicycloalkoxy, C_6-C_{18}-tricycloalkoxy, 1-indanyloxy, or 2-indanyloxy;

each of R^8, R^9, R^{10}, and R^{11}, independently of the others, is hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, halo, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, and alkoxy of 1 to 10 carbon atoms.

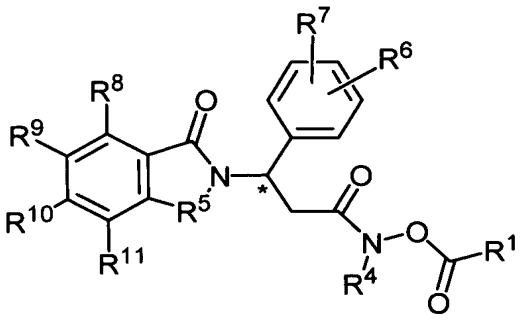
48. (New) The method of claim 46, wherein the compound is a compound of formula **I**.

49. (New) The method of claim 46, wherein the compound is a compound of formula **II**.

50. (New) The method of claim 46, wherein the compound is (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) propanoate; (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) acetate; (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) pentanoate; (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) benzoate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(1-oxoisoindolin-2-yl)propanoylamino) acetate; (3-[4-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-ethoxy-4-methoxyphenyl) propanoylamino)acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; N-acetyl-(3-(3-ethoxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; N-acetyl-(3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino) acetate; (3-[5-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) acetate; (3-(1,3-dioxobenzo[e]isoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl) propanoylamino)acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-phthalimido-propanoylamino)pyridine-3-carboxylate; (3-[4-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-cyclopentyloxy-4-methoxyphenyl)propanoylamino)acetate; (N-acetyl-3-[4-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-cyclopentyloxy-4-methoxyphenyl)propanoylamino)acetate; or (3-(3-ethoxy-4-methoxyphenyl)-3-(1-oxoisoindolin-2-yl)propanoylamino)acetate.

51. (New) A method of treating a disorder in a mammal comprising administering an effective amount of a compound of formula **I**, **II**, a pharmaceutically acceptable salt or solvate thereof, or a substantially chirally pure (R) or (S) isomer thereof, wherein said disorder is inflammatory disease, autoimmune disease, arthritis, rheumatoid arthritis, inflammatory bowel disease, Crohn's disease, aphthous ulcers, cachexia, graft versus host disease, asthma, adult respiratory distress syndrome, acquired immune deficiency syndrome, HIV, viral infection, dermal condition, tumor metastasis, tumor invasion, tumor growth, osteoarthritis, osteopenia, osteoporosis, periodontitis, gingivitis, corneal epidermal

inflammatory bowel disease, gastric ulceration, COPD, cancer, lupus, rheumatoid spondylitis, septic shock, sepsis, endotoxic shock, wasting, ulcerative colitis, multiple sclerosis, ENL in leprosy, or viral conjunctivitis:



I

wherein:

the carbon atom designated * constitutes a center of chirality;

R^4 is hydrogen or -(C=O)-R^{12};

each of R^1 and R^{12}, independently of each other, is alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridyl methyl, pyridyl, imidazoyl, imidazolylmethyl, or $CHR^*(CH_2)_nNR^*R^0$, wherein $R^*$and R^0, independently of the other, are hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridylmethyl, pyridyl, imidazoyl or imidazolylmethyl, and n = 0, 1, 2;

R^5 is C=O, CH_2, -CH_2-CO-, or SO_2;

each of R^6 and R^7, independently of the other, is nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 6 carbon atoms, alkoxy of 1 to 6 carbon atoms, cycloalkoxy of 3 to 8 carbon atoms, halo, bicycloalkyl of up to 18 carbon atoms, tricycloalkoxy of up to 18 carbon atoms, 1-indanyloxy, 2-indanyloxy, C_4-C_8-cycloalkylidenemethyl, or C_3-C_{10}-alkylidenemethyl; and

each of R^8, R^9, R^{10}, and R^{11} independently of the others, is

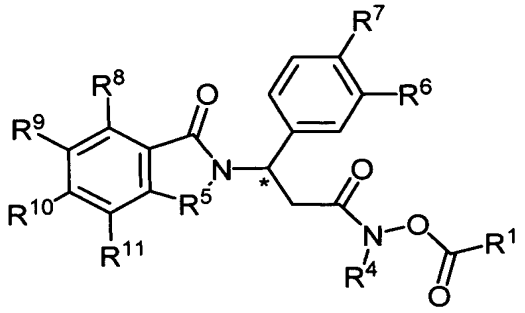
(i) hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, halo,

(ii) one of R^8, R^9, R^{10}, and R^{11} is acylamino comprising a lower alkyl, and the remaining of R^8, R^9, R^{10}, and R^{11} are hydrogen,

(iii) hydrogen if R^8 and R^9 taken together are benzo, quinoline, quinoxaline, benzimidazole, benzodioxole, 2-hydroxybenzimidazole, methylenedioxy, dialkoxy, or dialkyl,

(iv) hydrogen if R^{10} and R^{11}, taken together are benzo, quinoline, quinoxaline, benzimidazole, benzodioxole, 2-hydroxybenzimidazole, methylenedioxy, dialkoxy, or dialkyl, or

(v) hydrogen if R^9 and R^{10} taken together are benzo; or



II

wherein:

the carbon atom designated * constitutes a center of chirality;

R^4 is hydrogen or -(C=O)-R^{12},

where each of R^1 and R^{12}, independently of each other, is alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridyl, pyridyl methyl, imidazolyl, imidazoylmethyl, or $CHR^*(CH_2)_nNR^*R^0$

wherein $R^*$and R^0, independently of the other, are hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridylmethyl, pyridyl, imidazoyl or imidazolylmethyl, and n = 0, 1, 2;

R^5 is C=O or CH_2;

each of R^6 and R^7, independently of the other is alkoxy of 1 to 8 carbon atoms, cycloalkoxy of 3 to 6 carbon atoms; C_4-C_6-cycloalkylidenemethyl, C_2-C_{10}-alkylidenemethyl, C_6-C_{18}-bicycloalkoxy, C_6-C_{18}-tricycloalkoxy, 1-indanyloxy, or 2-indanyloxy;

each of R^8, R^9, R^{10}, and R^{11}, independently of the others, is hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, halo, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, and alkoxy of 1 to 10 carbon atoms.

52. (New) The method of claim 51, wherein the compound is a compound of formula **I**.

53. (New) The method of claim 51, wherein the compound is a compound of formula **II**.

54. (New) The method of claim 51, wherein the compound is (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) propanoate; (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) acetate; (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) pentanoate; (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) benzoate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(1-oxoisoindolin-2-yl)propanoylamino) acetate; (3-[4-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-ethoxy-4-methoxyphenyl) propanoylamino)acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; N-acetyl-(3-(3-ethoxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino)acetate; N-acetyl-(3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino) acetate; (3-[5-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) acetate; (3-(1,3-dioxobenzo[e]isoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl) propanoylamino)acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-phthalimido-propanoylamino)pyridine-3-carboxylate; (3-[4-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-cyclopentyloxy-4-methoxyphenyl)propanoylamino)acetate; (N-acetyl-3-[4-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-cyclopentyloxy-4-methoxyphenyl)propanoylamino)acetate; or (3-(3-ethoxy-4-methoxyphenyl)-3-(1-oxoisoindolin-2-yl)propanoylamino)acetate.

55. (New) The method of claim 51, wherein said dermal condition is psoriasis or atopic dermatitis.

56. (New) The method of claim 51, wherein said disorder is a viral infection.

57. (New) The method of claim 56, wherein said viral infection is HIV.

58. (New) The method of claim 51, wherein said disorder is viral conjunctivitis.

59. (New) The method of claim 51, wherein said disorder is cancer.

60. (New) The method of claim 51, wherein said disorder is an inflammatory disease.

61. (New) The method of claim 51, wherein said disorder is an autoimmune disease.

62. (New) The method of claim 51, wherein said disorder is rheumatoid arthritis.

63. (New) The method of claim 51, wherein said disorder is inflammatory bowel disease.

64. (New) The method of claim 51, wherein said disorder is Crohn's disease.

65. (New) The method of claim 51, wherein said disorder is asthma.

66. (New) The method of claim 51, wherein said disorder is adult respiratory distress syndrome.

67. (New) The method of claim 51, wherein said disorder is COPD.

68. (New) The method of claim 51, wherein said disorder is graft versus host disease.

69. (New) The method of claim 51, wherein said disorder is lupus.

70. (New) The method of claim 51, wherein said disorder is cachexia.